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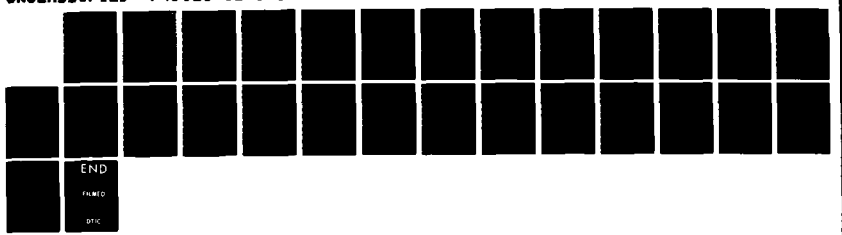

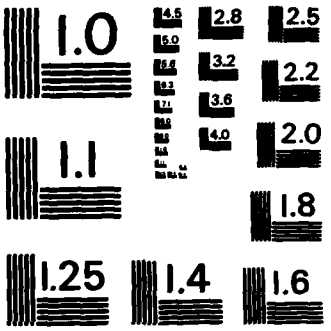

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COVARIATE MEASUREMENT ERROR IN LOGISTIC REGRESSION

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Abstract

In a logistic regression model when covariates are subject to measurement error the naive estimator, obtained by regressing on the observed covariates, is asymptotically biased. We introduce a bias-adjusted estimator and two estimators appropriate for normally distributed measurement errors; a functional maximum likelihood estimator and an estimator which exploits the consequences of sufficiency. The four proposals are studied asymptotically under conditions which are appropriate when the measurement error is small. A small Monte-Carlo study illustrates the superiority of the measurement-error estimators in certain situations.

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Key words and Phrases. Errors-in-variables, functional maximum likelihood, logistic regression, measurement error, sufficiency.

1. Introduction and Motivation.

Logistic regression is the most used form of binary regression (see Berkson, 1951; Cox, 1970; Efron, 1975; Pregibon, 1981). Independent observations (y_i, x_i) are observed where (x_i) are fixed p-vector predictors and (y_i) are Bernoulli variates with

$$\Pr\{y_i = 1 | x_i\} = F(x_i^T \beta_o) \triangleq (1 + \exp(-x_i^T \beta_o))^{-1} \quad . \tag{1.1}$$

Subject to regularity conditions, the large sample distribution of the maximum likelihood estimator of β_o is approximately normal with mean zero and covariance matrix $(1/n)S_n^{-1}(\beta_o)$, where $S_n(\cdot)$ is defined for $\gamma \in R^p$ as

$$S_n(\gamma) = n^{-1} \sum_1^n F^{(1)}(x_i^T \gamma) x_i x_i^T \tag{1.2}$$

Motivation for our paper comes from the Framingham Heart Study (Gordon and Kannel (1968)), a prospective study of the development of cardiovascular disease. This ongoing investigation has had an important impact on the epidemiology of heart disease. Much of the analysis is based on the logistic regression model with y an indicator of heart disease and x a vector of baseline risk factors such as systolic blood pressure, serum cholesterol, smoking, etc. It is well-known that many of these baseline predictors are measured with substantial error, e.g. systolic blood pressure. When a person's "true" blood pressure is defined as a long-term average then individual readings are subject to temporal as well as reader-machine variability. In one group of 45-54 year old Framingham males it was estimated that one fourth of the observed variability in blood pressure readings was due to within subject variability. The second author was asked by some Framingham investigators to assess the impact of such substantial measurement error and to suggest alternatives to usual logistic regression which account for this error. The present study is an out growth of these questions.

When covariates are measured with error the usual logistic regression estimator of β_o is asymptotically biased; see Clark (1982) and Michalik and Tripathi (1980). As a consequence of bias there is generally a tendency to underestimate the disease probability for high risk cases and overestimate for low risk; it will be said that measurement error attenuates predicted probabilities. Also, bias creates a problem with hypothesis testing; in Section 2 it is shown that the usual asymptotic tests for individual regression components can have level higher than expected. An example of this occurs in an unbalanced two-group analysis of covariance where interest lies in testing for treatment effect but the covariable is measured with error.

The severity of these problems depends, of course, on the magnitude of the measurement error. In some situations ordinary logistic regression might perform satisfactorily. However, when measurement error is substantial, alternative procedures are necessary. In addition, the availability of techniques which correct for measurement error can make clear the need for better measurement, e.g., more blood pressure readings over a period of days.

In Section 2 our measurement error model is defined and the asymptotic bias in the usual logistic regression estimator is studied. Section 3 presents some alternative estimators; results of a Monte Carlo study are outlined in Section 4; proofs of the asymptotic results are given in Section 5.

Until recently the study of measurement error models has focused primarily on linear models; see the review article by Madansky (1959) and the papers by Fuller (1980) and Gleser (1981). Interest in nonlinear models is increasing with recent contributions by Prentice, 1982; Wolter and Fuller, 1982a and 1982b; Carroll, Spiegelman, Lan, Bailey, and Abbott, 1984; Armstrong, 1984; Amemiya, 1982; and Clark, 1982. Of these articles Clark (1982) and Carroll et. al. (1984) focus specifically on logistic regression. The asymptotic methods employed in this paper are similar to those used by Wolter and Fuller (1982a)

and Amemiya (1982) in their studies of nonlinear functional relationships.

2. A Measurement Error Model for Logistic Regression.

2.1. The Model.

Our measurement error model starts with (1.1), but rather than observing the p-vector x_i we observe

$$X_i = x_i + \sigma v_i, \qquad \text{where} \quad v_i = \Sigma^{\frac{1}{2}} \varepsilon_i \ . \tag{2.1}$$

In (2.1) $\Sigma^{\frac{1}{2}}$ is the square root of a symmetric semi-positive definite matrix Σ scaled so that $\|\Sigma\| = 1$ and (ε_i) are independent and identically distributed random vectors with zero mean and identity covariance; also ε_i is independent of y_i, $i=1,\cdots,n$. The scale factor σ dictates the magnitude of the measurement error, e.g. if X_i is a mean of m independent replicate measurements of x_i then $\sigma \propto m^{-\frac{1}{2}}$. The asymptotic theory presented in this paper requires that $\sigma \to 0$ as $n \to \infty$, i.e. large sample, small-measurement-error asymptotics. The asymptotics are relevant for two situations: (i) X_i is an average of m independent measurements of x_i, in which case the Central Limit Theorem suggests that (ε_i) should be viewed as normal random variates and (ii) when measurement error is small but nonnegligible. In the latter case the moments of order greater than two of (ε_i) generally differ from those of a normal variate.

Our methods of correcting for bias require knowledge of the error covariance matrix $V \overset{\Delta}{=} \sigma^2\Sigma$. Since this information is seldom available all asymptotic results are derived for the case in which V is replaced by an estimator $\hat{V}$ satisfying

$$n^{\frac{1}{2}} (\hat{V} - V) = O_p(\sigma^2) \ . \tag{2.2}$$

Condition (2.2) is satisfied, for example, when V is estimated by replication. It is convenient to write $\hat{V} = \hat{\sigma}^2\hat{\Sigma}$ where $\hat{\sigma}^2 = \|\hat{V}\|$ and $\hat{\Sigma} = \hat{V}/\|\hat{V}\|$; note that (2.2) then implies $n^{\frac{1}{2}}(1 - \hat{\sigma}^2/\sigma^2) = O_p(1)$.

2.2 The Effects of Measurement Error.

Our investigation starts with a study of the estimator obtained by regressing y_i on the observed X_i. This estimator, to be called $\hat{\beta}$, maximizes

$$L_n(\gamma) \triangleq n^{-1}\sum_1^n \left\{ y_i \log F(c_i^T\gamma) + (1-y_i)\log F(-c_i^T\gamma)\right\} \tag{2.3}$$

and satisfies

$$\sum_1^n (y_i - F(c_i^T\hat{\beta}))c_i = 0 , \tag{2.4}$$

when $c_i = X_i$, $i=1,\ldots,n$. Our interest lies in the behavior of $\hat{\beta}$ as $\max(\sigma,n^{-1}) \to 0$. In addition to assumptions on the errors ε_i, some design conditions are necessary to insure weak consistency of $\hat{\beta}$. We shall work with the following assumptions:

(C1) $G_n(\gamma)$ converges pointwise to a function $G(\gamma)$ possessing a unique maximum at β_o where $G_n(\cdot)$ is defined as

$$G_n(\gamma) \triangleq n^{-1}\sum_1^n \left\{ F(x_i^T\beta_o)\log F(x_i^T\gamma) + F(-x_i^T\beta_o)\log F(-x_i^T\gamma)\right\};$$

(C2) $\sum_1^n (\|x_i\|)^2 = o(n^2)$;

(C3) $E(\|\varepsilon_1\|) < \infty$.

(C1) is an assumption of convenience since for each n, $G_n(\cdot)$ is concave with a maximum at β_o. Weaker conditions could thus be employed by studying subsequences of $G_n(\cdot)$; see Theorem 10.9, Rockafellar (1970).

Consistency of $\hat{\beta}$ is proved in Theorem 5.1 ; this result is necessary to establish the following asymptotic expansion which is crucial to our investigation. Theorem 1 gives conditions such that with $N(\sigma,n) = \max(\sigma^2,n^{-\frac{1}{2}})$,

$$\hat{\beta} = \beta_o + n^{-\frac{1}{2}}S_n^{-1}(\beta_o)Z_n + \sigma^2 S_n^{-1}(\beta_o)(J_{n,1} + J_{n,2})\beta_o + o_p(N(\sigma,n)), \tag{2.5}$$

where $$Z_n = n^{-\frac{1}{2}}\sum_1^n (y_i - F(x_i^T\beta_o))x_i \ ;$$

$$J_{n,1} = -(2n)^{-1}\sum_1^n F^{(2)}(x_i^T\beta_o)x_i\beta_o^T\Sigma \ ;$$

$$J_{n,2} = -n^{-1} \sum_{1}^{n} F^{(1)}(x_i^T \beta_o) I \quad .$$

Theorem 1. (Asymptotic expansion of $\hat{\beta}$). Assume that $\hat{\beta}$ is a consistent estimator of β_o satisfying (2.4). Also assume:

(A1) There exist a positive definite matrix M, $\delta > 0$, and $N_o < \infty$, such that $S_n(\gamma) \geq M$ whenever $n \geq N_o$ and $\|\gamma - \beta_o\| \leq \delta$;

(A2) $n^{-1} \sum_{i}^{n} \|x_i\|^2 \longrightarrow x^2 < \infty$, $\max_{1 \leq i \leq n} \|x_i\| = o(\sigma^{-2})$;

(A3) $E(\varepsilon_1) = 0$, $E(\varepsilon_1 \varepsilon_1^T) = I$, $E(\|\varepsilon_1\|^{2+\alpha}) \leq B$ for some $\alpha > 0$, $B < \infty$.

Then $\hat{\beta}$ has the expansion given in (2.5).

Note that assumptions (A1) and (A2) are sufficient to insure asymptotic normality for Z_n by an appeal to the Lindeberg Central Limit Theorem. Thus Theorem 1 indicates that with $\lambda = n^{\frac{1}{2}}\sigma^2$ we can expect $n^{\frac{1}{2}}(\hat{\beta} - \beta_o)$ to be approximately normally distributed with mean $\lambda S_n^{-1}(\beta_o)(J_{n,1} + J_{n,2})\beta_o$ and covariance $S_n^{-1}(\beta_o)$, when n is large and σ is small. When X_i is a mean of m replicates, $\sigma^2 \propto m^{-1}$ and λ describes the relationship between the sample size and the rate of replication. The asymptotic bias obviously decreases with increasing replication.

We can use expansion (2.5) to construct a corrected estimator, $\hat{\beta}_c$, which has smaller asymptotic bias. Before doing so we comment on the problems with $\hat{\beta}$ alluded to in the introduction.

Bias and attenuation. Consider simple logistic regression through the origin with $\beta_o > 0$. One expects to see attenuation, i.e., a negative first order bias term. For most designs this is true. Somewhat surprisingly and completely at odds with the linear regression case, $S_n^{-1}(\beta_o)(J_{n,1} + J_{n,2})\beta_o$ can be positive. One design in which this occurs arises when most cases have very high or very low risk, i.e. $|x_i^T\beta_o|$ is large for most i.

Hypothesis Testing. Consider a two-group analysis of covariance, $x_i^T = (1, (-1)^i, d_i)$, $\beta_o = (\beta_0, \beta_1, \beta_2)$. The covariable d_i is measured with error variance σ^2. Often interest lies in testing hypotheses about the treatment effect β_1. A standard method to test $\beta_1 = 0$ is to compute its logistic regression estimate compared to the usual estimate of its asymptotic standard error. When the asymptotics of Theorem 1 are relevent and $n^{\frac{1}{2}}\sigma^2 \to \lambda > 0$, this test approaches its nominal level only if the second component of $S_n^{-1}(\beta_o)(J_{n,1} + J_{n,2})\beta_o$ approaches zero. Letting s_2 denote the second row of $S_n^{-1}(\beta_o)$ this is achieved only if

$$n^{-1}\sum_1^n s_2^T x_i F^{(2)}(x_i^T\beta_o)\sigma^2\beta_2^2 \to 0.$$

This will not hold in the common epidemiologic situation in which the true covariables are not balanced across the two treatments. Thus, when substantial measurement error occurs in a nonrandomized study, there will be bias in the asymptotic levels of the usual tests.

3. Accounting for Measurement Error.

In this section three alternative approaches to estimation are studied. The first is based on expansion (2.5) and is distribution-free in the sense that only moment assumptions are made about the measurement errors. The second two methods are based on an assumption of normally distributed errors; their asymptotic properties are then studied under more general conditions.

3.1 Adjusting for Bias in $\hat{\beta}$.

Write $b_n = S_n^{-1}(\beta_o)(J_{n,1} + J_{n,2})\beta_o$ and $\hat{b}_n = \hat{S}_n^{-1}(\hat{\beta})(\hat{J}_{n,1} + \hat{J}_{n,2})\hat{\beta}$

where

$$\hat{S}_n(\gamma) = n^{-1}\sum_1^n F^{(1)}(X_i^T\gamma)X_iX_i^T; \tag{3.1}$$

$$\hat{J}_{n,1} = -(2n)^{-1}\sum_1^n F^{(2)}(X_i^T\hat{\beta})X_i\hat{\beta}^T\hat{\epsilon};$$

$$\hat{J}_{n,2} = -n^{-1}\sum_1^n F^{(1)}(X_i^T\hat{\beta})\hat{\epsilon};$$

$\hat{b}_n$ depends only on the observed data and, under the conditions of Theorem 1 and (2.2), approximates b_n in the sense that $\hat{b}_n - b_n = o_p(1)$ as $\min(n, \sigma^{-1}) \to \infty$. This result suggests that the bias-corrected estimator $\hat{\beta}_c \triangleq \hat{\beta} - \partial^2\hat{b}_n$ should have smaller asymptotic bias for large n and small σ. We state these results as a theorem.

Theorem 2. Assume the conditions of Theorem 1 and (2.2). Then

$$\hat{\beta}_c = \beta_o + n^{-\frac{1}{2}}S_n^{-1}(\beta_o)Z_n + o_p(N(\sigma,n)).$$

Remarks. In Section 5, Theorem 2 is proved using the following characterization of $\hat{\beta}_c$: Note that $\hat{\beta}_c = (I - \partial^2\hat{B}_n)\hat{\beta}$ where $\hat{B}_n = \hat{S}_n^{-1}(\hat{\beta})(\hat{J}_{n,1} + \hat{J}_{n,2})$. Since $X_i^T\hat{\beta} = X_i^T(I - \partial^2\hat{B}_n)^{-1}\hat{\beta}_c$ it follows that $\hat{\beta}_c$ maximizes (2.3) when $c_i = \hat{x}_{i,c}$, defined as

$$\hat{x}_{i,c} = X_i + \partial^2(I - \partial^2\hat{B}_n^T)^{-1}\hat{B}_n^TX_i\ . \tag{3.2}$$

In this sense $\hat{\beta}_c$ is a type of two-stage estimator obtained by doing logistic regression with $\hat{x}_{i,c}$ replacing X_i.

The estimator $\hat{\beta}_c$ is not unbiased, just less biased. The Monte Carlo study of Section 4 shows that in some realistic sampling situations the reduction in bias is substantial.

unlike linear regression in which the errors-in-variables functional maximum likelihood estimator is consistent when V is known.

Our final estimator starts with an assumption of normal errors and exploits the consequences of sufficiency. Given $\sigma^2\Sigma$ and β_o, a sufficient statistic for estimating x_i is $\bar{c}_i(\beta_o) = X_i + \sigma^2(y_i - \frac{1}{2})\Sigma\beta_o$; it follows that the distribution of y_i given $\bar{c}_i(\beta_o)$ does not depend on x_i. The reason for using this particular sufficient statistic is that

$$P\{y_i = 1|\bar{c}_i(\beta_o)\} = F(\bar{c}_i^T(\beta_o)\beta_o) \tag{3.4}$$

and hence the score equation

$$\sum_1^n (y_i - F(\bar{c}_i^T(\beta)\beta))\bar{c}_i(\beta) = 0 \tag{3.5}$$

is unbiased for β_o. Equation (3.5) can have multiple solutions not all which produce a consistent sequence of estimators. Since $\bar{c}_i(\beta)$ also depends on the unknown matrix $\sigma^2\Sigma$ we propose the following modification: Let

$$\hat{x}_{i,s} = X_i + \hat{\sigma}^2(y_i - \tfrac{1}{2})\hat{\Sigma}\hat{\beta} \tag{3.6}$$

and define $\hat{\beta}_s$, the sufficiency estimator, as the maximizer of (2.3) when c_i is replaced by $\hat{x}_{i,s}$. This estimator is consistent under (C1) - (C3) and (2.2) and has the expansion given in the next theorem.

Theorem 4. Assume the conditions of Theorem 1 and (2.2). Then

$$\hat{\beta}_s = \beta_o + n^{-\frac{1}{2}}S_n^{-1}(\beta_o)Z_n + o_p(N(\sigma,n)).$$

Remarks. 1. Theorem 4 does not require the assumption of normal measurement error. Also, $\hat{\beta}$ can be replaced by any consistent estimator in the definition of $\hat{x}_{i,s}$. The effects of nonnormal measurement error and our particular choice of $\hat{x}_{i,s}$ become apparent only when $\hat{\beta}_s$ is expanded through terms of order $N^2(\sigma,n)$. This analysis is lengthy and is not presented here.

3.2 Normal Measurement Error.

When measurement error is present there is an added source of variation which is not accounted for by model (1.1). We now expand this model by assuming that (ε_i) are normally distributed, an assumption which is not unreasonable in some situations. The functional log-likelihood for estimating β_o and $x_1,\ldots,x_n$ is then

$$\sum_1^n \left\{y_i \log(F(x_i^T\beta)) + (1-y_i)\log(F(-x_i^T\beta)) - (2\sigma^2)^{-1}(X_i - x_i)^T\Sigma^{-1}(X_i - x_i)\right\}. \qquad (3.3)$$

The vectors $\tilde{\beta}_f$, $\tilde{c}_i$ maximizing (3.3) satisfy

$$\sum_1^n (y_i - F(\tilde{c}_i^T\tilde{\beta}_f)\tilde{c}_i = 0 \ ;$$

$$\tilde{c}_i = X_i + (y_i - F(\tilde{c}_i^T\tilde{\beta}_f))\sigma^2\Sigma\tilde{\beta}_f \qquad i = 1,\ldots,n.$$

There are two problems with this estimator; it depends on the unknown matrix $\sigma^2\Sigma$ and solving for $\tilde{\beta}_f$ and $(\tilde{c}_i)$ is difficult. For these reasons we suggest a modified version of $\tilde{\beta}_f$. Noting the form of $\tilde{c}_i$ we let

$$\hat{x}_{i,f} = X_i + (y_i - F(X_i^T\hat{\beta}))\hat{\sigma}^2\hat{\Sigma}\hat{\beta} \qquad (3.4)$$

and define $\hat{\beta}_f$ as the estimator obtained by maximizing (2.3) with $c_i = \hat{x}_{i,f}$; $\hat{\beta}_f$ is consistent under (C1) - (C3) and (2.2) and has an asymptotic expansion given in the next theorem.

Theorem 3. Assume the conditions of Theorem 1 and (2.2). Then

$$\hat{\beta}_f = \beta_o + n^{-\frac{1}{2}}S_n^{-1}(\beta_o)Z_n + \sigma^2 S_n^{-1}(\beta_o)J_{n,1}\beta_o + o_p(N(\sigma,n)).$$

Remarks. The functional maximum likelihood estimator, like $\hat{\beta}$, has a first order bias. The bias term is not due to our one-step modification nor to $\hat{V}$; this fact is evident from the proof of Theorem 5.2. Logistic regression is thus

2. It is possible to define a sufficiency estimator for a large class of measurement error models. In particular we have in mind the generalized linear models with canonical link functions (McCullagh and Nelder, 1983). A complete exposition of this theory will appear elsewhere.

In the next section results from a small Monte Carlo study are presented.

4. Monte Carlo

We conducted a small simulation experiment to determine the relative merits of the four estimators $\hat{\beta}$, $\hat{\beta}_c$, $\hat{\beta}_f$, and $\hat{\beta}_s$.

The model for the study was

$$\Pr\{y_i = 1|d_i\} = \alpha + \beta d_i, \quad i=1,\ldots,n. \tag{4.1}$$

We considered these sampling situations where χ^2_1 denotes a chi-squared random variable with one degree of freedom:

(I) $(\alpha,\beta) = (-1.4,1.4)$, $(d_i) \sim$ Normal $(0,\sigma_d^2 = .10)$, $n = 300, 600$;

(II)$(\alpha,\beta) = (-1.4,1.4)$, $(d_i) \sim \sigma_d(\chi^2_1 - 1)/\sqrt{2}$, $\sigma_d^2 = .10$, $n = 300, 600$;

For both cases, the measurement error variance τ^2 was one third the variance of the true predictors ($\tau^2 = \sigma_d^2/3$). For each case, we considered two sampling distributions for the measurement errors (ϵ_i): (a) Normal$(0,\tau^2)$ and (b) a contaminated normal distribution, which is Normal$(0,\tau^2)$ with probability 0.90 and Normal$(0,25\tau^2)$ with probability 0.10.

We believe these two sampling situations are realistic, but their representativeness is limited by the size of the study. The sample sizes $n = 300, 600$ may seem large, but our primary interest is in larger epidemiologic studies where such sample sizes are common. For example, Clark (1982) was motivated by a study with $n = 2580$, Hauck (1983) quotes a partially completed study with $n \geq 340$, and we have analyzed Framingham data for males aged 45-54 with $n = 589$.

Furthermore, the results of the study suggest that correcting for measurement error in most small sample situations is unwarrented.

The values of the predictor variance σ_d^2 and the measurement error variance τ^2 are similar to those found in the Framingham cohort mentioned in the previous paragraph when the predictor was $\log_e\{(\text{systolic blood pressure}-75)/3\}$, a standard transformation. The ratio $\tau^2/\sigma_d^2 = 1/3$ is not uncommon; Clark finds a similar ratio in her study of triglyceride. The choice of (α,β) comes from Framingham data as well. All experiments were repeated 100 times.

In each experiment, we sampled two independent measurements $(D_{i,1}, D_{i,2})$ of each d_i; the observed covariate was $X_i = (1, \bar{D}_i)^T$, where $\bar{D}_i = (D_{i,1} + D_{i,2})/2$. The matrix $\sigma^2\Sigma$ has only one non-zero entry which was estimated by the sample variance of $(D_{i,1} - D_{i,2})/2$.

In addition to the four estimators presented in this paper we included in the study a proposal due to Clark (1982). She suggests the estimator $\hat{\beta}_N$ obtained by maximizing (2.3) when c_i is replaced by $\hat{x}_{i,N} = X_i - \hat{\sigma}^2\hat{\Sigma}\hat{\Sigma}_X^{-1}(X_i - \hat{\mu})$ where $\hat{\mu}$ and $\hat{\Sigma}_X$ are the sample mean and covariance of the observed data. Motivation for this estimator derives from an assumption of normal errors and normal covariates. In this case $E(x_i|X_i) = X_i - \sigma^2\Sigma\Sigma_X^{-1}(X_i - \mu)$ and hence $\hat{x}_{i,n}$ is a natural estimator of x_i. Theorems 5.1 and 5.2 can be used to prove consistency and derive an asymptotic expansion for this estimator. Like $\hat{\beta}$ and $\hat{\beta}_f$, $\hat{\beta}_N$ has a non-zero first order bias although it is too lengthy to present here.

Sweeping conclusions cannot be made from such a small study. However, we can make the following qualitative suggestions. First $\hat{\beta}$ is less variable but more biased than the others; sample sizes such as $n = 600$ as in the study or Clark's $n = 2580$ are such that bias dominates and hence are candidates for using corrected estimators; an opposite conclusion holds for small sample sizes where

variance dominates. A second suggestion from the tables is that when $\hat{\beta}$ loses efficiency (Case I(b), II(b) and when n = 600), the corrected estimators perform quite well.

Both $\hat{\beta}_s$ and $\hat{\beta}_f$ were defined via an assumption of normal errors yet they also performed well when the errors were contaminated normal, (Cases I(b), II(b)). Clark's estimator proved to be sensitive to the assumption of normal covariates; $\hat{\beta}_N$ performed very well in our study when the predictors were normally distributed, but it did have a noticeable drop in efficiency when the predictors were highly skewed (Case II). Finally, the corrected estimator $\hat{\beta}_c$, which was derived with no distributional assumptions for either the predictors or errors, performed well throughout the study.

In summary, the Monte Carlo results suggest that the estimators $\hat{\beta}_c$, $\hat{\beta}_f$, $\hat{\beta}_s$ and Clark's $\hat{\beta}_N$ are useful alternatives to $\hat{\beta}$ when covariates are measured with error. The pressing practical problem now appears to be to delineate those situations in which ordinary logistic regression should be corrected for its bias. Studies of inference and more detailed comparisons of alternative estimators will be enhanced by the identification of those problems where measurement error severely affects the usual estimation and inference.

5. Proofs of Theorems

Consider the estimator $\tilde{\beta}$ obtained by maximizing (2.3) when c_i is replaced with $\tilde{x}_i$ where

$$\tilde{x}_i = x_i + \sigma v_i + \sigma^2 g_{in}. \tag{5.1}$$

In Theorem 5.1 we prove weak consistency of $\tilde{\beta}$ under conditions (C1), (C2), (C3) and

(P1) $$\sum_1^n \|g_{in}\|^2 = O_p(n) .$$

In Theorem 5.2 an asymptotic expansion for $\tilde{\beta}$ is given. The consistency and

asymptotic expansions of $\hat{\beta}$, $\hat{\beta}_c$, $\hat{\beta}_f$, and $\hat{\beta}_s$ follow from these general results by noting that X_i, $\hat{x}_{i,c}$, $\hat{x}_{i,f}$, and $\hat{x}_{i,s}$ all have the representaton given in (5.1). We remind the reader that all the asymptotic expressions hold as $\max(\sigma, n^{-1}) \to 0$.

Theorem 5.1 (Consistency). Assume (C1), (C2), (C3), and (P1); then $\tilde{\beta} - \beta_o = o_p(1)$.

Proof. Define $\tilde{L}_n(\gamma)$ to be the function obtained by taking $c_i = \bar{x}_i$ in (2.3). The identity $\log(F(t)/(1-F(t))) = t$ is used to show $\tilde{L}_n(\gamma) - G_n(\gamma) = R_{n,1} + R_{n,2}$ where

$$R_{n,1} = n^{-1} \sum_1^n (y_i - F(x_i^T \beta_o)) x_i^T \gamma \ ;$$

$$R_{n,2} = n^{-1} \sum_1^n \left\{ y_i (\bar{x}_i^T \gamma - x_i^T \gamma) + \log F(-\bar{x}_i^T \gamma) - \log F(-x_i^T \gamma) \right\} .$$

Under (C2), $R_{n,1}$ has mean zero and asymptotically negligible variance; also by (C3) and (P1),

$$\|R_{n,2}\| \le 2\sigma \|\gamma\| n^{-1} \sum_1^n \|v_i + \sigma g_{in}\| = o_p(1) .$$

Consequently (C1) implies that $\tilde{L}_n(\cdot)$ converges pointwise in probability to $G(\cdot)$. An appeal to *Theorem II.1 of Anderson and Gill (1982)* concludes the proof.

The consistency results follow by applying Theorem 5.1 first to $\tilde{\beta}$, ($g_{in} = 0$) and then to $\hat{\beta}_c$, $\hat{\beta}_f$, and $\hat{\beta}_s$. Next we derive the asymptotic expansions for these estimators.

Theorem 5.2 (Asymptotic expansion). Assume (P1) and the conditions of Theorem 1; then

$$\tilde{\beta} = \beta_o + n^{-\frac{1}{2}} S_n^{-1}(\beta_o) Z_n + \sigma^2 S_n^{-1}(\beta_o) \left\{ (J_{n,1} + J_{n,2}) \beta_o + b_{n,3} + b_{n,4} \right\} + o_p(N(\sigma, n)),$$

where $b_{n,3} = n^{-1} \sum_1^n (y_i - F(x_i^T \beta_o)) g_{in}$,

$$b_{n,4} = -n^{-1} \sum_{1}^{n} F^{(1)}(x_i^T\beta_o)x_i g_{in}^T\beta_o,$$

$S_n(\cdot)$ is given in (1.2), and Z_n, $J_{n,1}$, and $J_{n,2}$ are defined in (2.5).

Theorem 5.2 is proved with a series of lemmas. First we show how Theorems 1-4 follow as corollaries. Theorem 1 is immediate since $g_{in} = 0$ for $\hat{\beta}$. For $\hat{\beta}_c$, $g_{in} = (\partial^2/\sigma^2)(I - \partial^2\hat{B}_n^T)^{-1}\hat{B}_n^T X_i$ where $\hat{B}_n = \hat{S}_n^{-1}(\hat{\beta})(\hat{J}_{n,1} + \hat{J}_{n,2})$. Assumptions (A2), (A3), Lemma 5.1, and (2.2) imply $b_{n,3} = o_p(1)$ and

$$\begin{aligned} -b_{n,4} &= n^{-1} \sum_{1}^{n} F^{(1)}(x_i^T\beta_o)x_i X_i^T\hat{B}_n(I - \partial^2\hat{B}_n)^{-1}\beta_o \\ &= S_n(\beta_o)\hat{B}_n\beta_o + o_p(1) \\ &= (J_{n,1} + J_{n,2})\beta_o + o_p(1), \end{aligned}$$

thus proving Theorem 2.

For $\hat{\beta}_f$, $g_{in} = (\partial^2/\sigma^2)(y_i - F(X_i^T\hat{\beta}))\hat{\Sigma}\hat{\beta}$ and (A2), (A3), Lemma 5.1, and (2.2) imply $b_{n,4} = o_p(1)$ and

$$\begin{aligned} b_{n,3} &= n^{-1} \sum_{1}^{n} (y_i - F(x_i^T\beta_o))^2\Sigma\beta_o + o_p(1) \\ &= -J_{n,2}\beta_o + o_p(1) ; \end{aligned}$$

Theorem 3 follows. Finally for $\hat{\beta}_s$, $g_{in} = (\partial^2/\sigma^2)(y_i - \tfrac{1}{2})\hat{\Sigma}\hat{\beta}$. (A2), (A3), Lemma 5.1 and (2.2) imply

$$\begin{aligned} b_{n,3} &= n^{-1} \sum_{1}^{n} (y_i - F(x_i^T\beta_o))(y_i - \tfrac{1}{2})\Sigma\beta_o + o_p(1) \\ &= -J_{n,2}\beta_o + o_p(1); \end{aligned}$$

$$\begin{aligned} b_{n,4} &= -n^{-1} \sum_{1}^{n} F^{(1)}(x_i^T\beta_o)(y_i - \tfrac{1}{2})x_i\beta_o^T\Sigma\beta_o + o_p(1) \\ &= -n^{-1} \sum_{1}^{n} F^{(1)}(x_i^T\beta_o)(F(x_i^T\beta_o) - \tfrac{1}{2})x_i\beta_o^T\Sigma\beta_o + o_p(1) \end{aligned}$$

$$= - J_{n,1}\beta_o + o_p(1).$$

In the last step we use the identity $F^{(2)}(t) = F^{(1)}(t)(1 - 2F(t))$. This proves Theorem 4. Notice that in deriving these results we used only the fact that $\hat{\beta} - \beta_o = o_p(1)$ thus the conclusions of Theorems 3 and 4 remain unchanged if $\hat{\beta}$ is replaced by any other consistent estimator in the definitions of $\hat{x}_{i,f}$ and $\hat{x}_{i,s}$. In particular this implies that the fully iterated versions of the functional and sufficiency estimators (provided consistent versions are chosen) also satisfy Theorems 3 and 4 respectively.

The proof of Theorem 5.2 starts with the following weak law.

Lemma 5.1. Let $u_1, u_2, \ldots$ be independent random vectors such that $E(u_i) = 0$ and $E(\|u_i\|^{1+\alpha}) \leq B$ for some $\alpha > 0$ and $B < \infty$. If $\sum_1^n |a_i| = O(n)$ and $\max_{1\leq i\leq n} (|a_i|/n) = o(1)$ then $n^{-1}\sum_1^n a_i u_i = o_p(1)$.

Proof. The proof of the lemma entails a routine verification of the assumptions of Theorem 5.23, Chung, (1974) and is not given here.

Lemma 5.2. Under the conditions of Theorem 1,

$$n^{-1}\sum_1^n (y_i - F(X_i^T\beta_o))X_i = n^{-\frac{1}{2}}Z_n + \sigma^2(J_{n,1} + J_{n,2})\beta_o + o_p(N(\sigma,n)).$$

Proof. $n^{-1}\sum_1^n (y_i - F(X_i^T\beta_o)X_i = T_{n,1} + T_{n,2}$ where

$$T_{n,1} = n^{-1}\sum_1^n (y_i - F(X_i^T\beta_o))x_i$$

$$T_{n,2} = \sigma n^{-1}\sum_1^n (y_i - F(X_i^T\beta_o))v_i.$$

A Taylor series expansion of $F(\cdot)$ shows that

$$T_{n,1} = n^{-\frac{1}{2}}Z_n + \sigma^2 J_{n,1}\beta_o + n^{-\frac{1}{2}}Q_{n,1,\sigma} + \sigma^2(D_{n,1} + R_{n,1})$$

where $$Q_{n,1,\sigma} = -\sigma n^{-\frac{1}{2}} \sum_1^n F^{(1)}(x_i^T\beta_o)v_i^T\beta_o x_i \ ;$$

$$D_{n,1} = -(2n)^{-1} \sum_1^n \{F^{(2)}(x_i^T\beta_o)((v_i^T\beta_o)^2 - \beta_o^T\Sigma\beta_o)x_i\};$$

$$R_{n,1} = -(2n)^{-1} \sum_1^n (F^{(2)}(\tilde{X}_i^T\beta_o) - F^{(2)}(x_i^T\beta_o))(v_i^T\beta_o)^2 x_i \ ;$$

and $\tilde{X}_i$ is on the line segment joining x_i to X_i. $Q_{n,1,\sigma}$ has mean zero and asymptotically negligible variance thus $n^{-\frac{1}{2}}Q_{n,1,\sigma} = o_p(n^{-\frac{1}{2}})$. Assumptions (A2) and (A3) and Lemma 5.1 are used to show $D_{n,1} = o_p(1)$. Also note that

$$\|R_{n,1}\| \le (2n)^{-1} \sum_1^n \|x_i\|(v_i^T\beta_o)^2 \min(1,\sigma|v_i^T\beta_o|) \le A_n B_n$$

where $$A_n = (n^{-1} \sum_1^n \|x_i\|^2(v_i^T\beta_o)^2)^{\frac{1}{2}};$$

$$B_n = (n^{-1} \sum_1^n (v_i^T\beta_o)^2 \min^2(1,\sigma|v_i^T\beta_o|))^{\frac{1}{2}}.$$

Assumptions (A2) and (A3) and Lemma 5.1 imply $A_n = 0_p(1)$ while (A3) and the fact that $\max(n^{-1},\sigma) \longrightarrow 0$ imply $B_n = o_p(1)$. It follows that $\sigma^2(D_{n,1} + R_{n,1}) = o_p(\sigma^2)$. Combining these results we get

$$T_{n,1} = n^{-\frac{1}{2}}Z_n + \sigma^2 J_{n,1}\beta_o + o_p(N(\sigma,n)). \tag{5.2}$$

Another Taylor series expansion of $F(\cdot)$ shows that

$$T_{n,2} = \sigma^2 J_{n,2}\beta_o + n^{-\frac{1}{2}}Q_{n,2,\sigma} + \sigma^2(D_{n,2} + R_{n,2})$$

where $$Q_{n,2,\sigma} = \sigma n^{-\frac{1}{2}} \sum_1^n (y_i - F(x_i^T\beta_o))v_i;$$

$$D_{n,2} = -n^{-1} \sum_1^n F^{(1)}(x_i^T\beta_o)(v_i v_i^T - \Sigma)\beta_o;$$

$$R_{n,2} = -n^{-1}\sum_{1}^{n}(F^{(1)}(\tilde{X}_i^T\beta_o) - F^{(1)}(x_i^T\beta_o))v_i v_i^T\beta_o ;$$

and $\tilde{X}_i$ lies on the line segment joining x_i to X_i. $Q_{n,2,\sigma}$, $D_{n,2}$, and $R_{n,2}$ are all $o_p(1)$; the proofs are analogous to those for $Q_{n,1,\sigma}$, $D_{n,1}$, and $R_{n,1}$ respectively. Consequently

$$T_{n,2} = \sigma^2 J_{n,2}\beta_o + o_p(N(\sigma,n)). \tag{5.3}$$

Combining (5.2) and (5.3) completes the proof of the lemma.

Lemma 5.3. Assume the conditions of Theorem 1 and (P1) and define $\tilde{H}_n(\gamma) = n^{-1}\sum_{1}^{n}(y_i - F(\tilde{x}_i^T\gamma))\tilde{x}_i$; then

$$\tilde{H}_n(\beta_o) = n^{-\frac{1}{2}}Z_n + \sigma^2((J_{n,1} + J_{n,2})\beta_o + b_{n,3} + b_{n,4}) + o_p(N(\sigma,n)).$$

Proof. $\tilde{H}_n(\beta_o) = W_{n,1} + W_{n,2} + W_{n,3} + W_{n,4}$

where $$W_{n,1} = n^{-1}\sum_{1}^{n}(y_i - F(X_i^T\beta_o))X_i ;$$

$$W_{n,2} = \sigma n^{-1}\sum_{1}^{n}(F(X_i^T\beta_o) - F(\tilde{x}_i^T\beta_o))(v_i + \sigma g_{in}).$$

$$W_{n,3} = \sigma^2 n^{-1}\sum_{1}^{n}(y_i - F(X_i^T\beta_o))g_{in} ;$$

$$W_{n,4} = n^{-1}\sum_{1}^{n}(F(X_i^T\beta_o) - F(\tilde{x}_i^T\beta_o))x_i .$$

Note that in light of (A2) and (P1) $\|W_{n,2}\| \le \sigma^3 n^{-1}\sum_{1}^{n}\|g_{in}\|(\|v_i\| + \sigma\|g_{in}\|) = o_p(\sigma^2)$. Also, $\|W_{n,3} - \sigma^2 b_{n,3}\| \le \sigma^2 n^{-1}\sum_{1}^{n}|F(x_i^T\beta_o) - F(X_i^T\beta_o)|\|g_{in}\| \le \|\beta_o\|\sigma^3 n^{-1}\sum_{1}^{n}\|v_i\|\|g_{in}\| \le \|\beta_o\|\sigma^3(n^{-1}\sum_{1}^{n}\|v_i\|^2)^{\frac{1}{2}}(n^{-1}\sum_{1}^{n}\|g_{in}\|^2)^{\frac{1}{2}} = o_p(\sigma^2)$, using (A3) and (P1). One term in a Taylor series expansion of $F(\cdot)$ and Lemma 5.1, (A2), and (P1) show that

$$\|W_{n,4} - \sigma^2 b_{n,4}\| \le \sigma^2 \|\beta_o\|^2 n^{-1} \sum_1^n (\sigma\|v_i\| + \sigma^2\|g_{in}\|)\|x_i\|\|g_{in}\|$$

$$\le \sigma^2 \|\beta_o\|^2 \Big\{ \sigma n^{-1} \sum_1^n \|v_i\|\|x_i\|\|g_{in}\| + \sigma^2 n^{-1} \sum_1^n \|x_i\|\|g_{in}\|^2 \Big\}$$

$$\le \sigma^2 \|\beta_o\|^2 \Big\{ \sigma (n^{-1} \sum_1^n \|v_i\|^2\|x_i\|^2)^{\frac{1}{2}} (n^{-1} \sum_1^n \|g_{in}\|^2)^{\frac{1}{2}} +$$

$$\sigma^2 \Big(\max_{1\le i\le n} \|x_i\| \Big) n^{-1} \sum_1^n \|g_{in}\|^2 \Big\}$$

$$= o_p(\sigma^2) .$$

An expansion for $W_{n,1}$ is given in Lemma 5.2. Combining the above results proves the Lemma.

Lemma 5.4. Assume P1 and the conditions of Theorem 1, then

$$\tilde{\beta} - \beta_o = O_p(N(\sigma,n)).$$

Proof. Let $\tilde{H}_n(\cdot)$ be the function defined in Lemma 5.3. Consider the real-valued function of γ defined as $\tilde{J}_n(\gamma) = \tilde{H}_n^T(\gamma)(\tilde{\beta} - \beta_o)$. The Mean Value Theorem proves the existence of some $\bar{\beta}$ on the line segment joining $\tilde{\beta}$ to β_o such that

$$\tilde{H}_n^T(\beta_o)(\tilde{\beta} - \beta_o) = (\tilde{\beta} - \beta_o)^T \bar{S}_n(\bar{\beta})(\tilde{\beta} - \beta_o),$$

where $$\bar{S}_n(\gamma) = n^{-1} \sum_1^n F^{(1)}(\tilde{x}_i^T\gamma)\tilde{x}_i\tilde{x}_i^T .$$

It follows that $\|\tilde{\beta} - \beta_o\| \le \|\tilde{H}_n(\beta_o)\| \lambda_{min}^{-1}(\bar{S}_n(\bar{\beta}))$ where $\lambda_{min}(A)$ = minimum eigen value of A. Under (A2), (A3), and (P1), $\bar{S}_n(\bar{\beta}) - S_n(\bar{\beta}) = o_p(1)$ hence by (A1), $P\{\lambda_{min}^{-1}(\bar{S}_n(\bar{\beta})) \le \lambda_{min}^{-1}(M)\} \to 1$; thus $\|\tilde{\beta} - \beta_o\|$ and $\|\tilde{H}_n(\beta_o)\|$ have the same order which, from Lemma 5.3, is $O_p(N(\sigma,n))$.

We are now in a position to prove Theorem 6.2.

Proof of Theorem 6.2. By definition $n^{-1}\sum_{1}^{n}(y_i - F(\tilde{x}_i^T\tilde{\beta}))\tilde{x}_i = 0$; expanding $F(\cdot)$ in a Taylor series shows that $\tilde{S}(\tilde{\beta} - \beta_o) = \tilde{H}_n(\beta_o)$ where

$$\tilde{S} = n^{-1}\sum_{1}^{n} F^{(1)}(x_i^T\bar{\beta}_i)\tilde{x}_i\tilde{x}_i^T$$

and for each i, $\|\bar{\beta}_i - \beta_o\| \le \|\tilde{\beta} - \beta_o\|$. (A2), (A3), (P1), and the conclusion of Lemma 5.4 are used to show $\tilde{S} - S_n(\beta_o) = o_p(1)$. The Theorem follows from Lemma 5.4.

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TABLES

These are the results of the Monte-Carlo study. "Efficiency" refers to mean squared error efficiency with respect to ordinary logistic regression.

CASE I(a)

$(\alpha, \beta) = (-1.4, 1.4)$, $(d_i) \sim N(0, \sigma_d^2 = .1)$, $(\varepsilon_i) \sim N(0, \sigma^2 = .\sigma_d^2/3)$.

	$\hat{\beta}$	$\hat{\beta}_c$	$\hat{\beta}_f$	$\hat{\beta}_N$	$\hat{\beta}_s$
n = 300 Bias	-0.21	-0.04	-0.05	-0.02	-0.06
Std. Dev.	0.52	0.61	0.61	0.61	0.60
Efficiency	100%*	85%	85%	84%	88%
n = 600 Bias	-0.22	-0.05	-0.05	-0.02	-0.06
Std. Dev.	0.33	0.38	0.38	0.38	0.38
Efficiency	100%*	108%	106%	107%	108%

CASE I(b)

Same as Case I(a) but measurement errors have the contaminated normal distribution.

n = 300 Bias	-0.49	-0.16	-0.19	0.02	-0.20
Std. Dev.	0.34	0.48	0.48	0.54	0.46
Efficiency	100%*	143%	139%	121%	143%
n = 600 Bias	-0.53	-0.20	-0.21	-0.03	-0.22
Std. Dev.	0.24	0.33	0.34	0.38	0.33
Efficiency	100%*	223%	215%	234%	216%

* By definition.

CASE II(a)

$(\alpha, \beta) = (-1.4, 1.4)$, $(d_i) \sim \sigma_d(\chi_1^2-1)/\sqrt{2}$, $\sigma_d^2 = 0.1$, $(\varepsilon_i) \sim N(0, \sigma^2 = \sigma_d^2/3)$.

	$\hat{\beta}$	$\hat{\beta}_c$	$\hat{\beta}_f$	$\hat{\beta}_N$	$\hat{\beta}_s$
n = 300 Bias	-0.28	-0.05	-0.07	0.10	-0.08
Std. Dev.	0.47	0.58	0.57	0.66	0.56
Efficiency	100%*	90%	91%	69%	93%
n = 600 Bias	-0.27	-0.03	-0.04	0.11	-0.05
Std. Dev.	0.33	0.41	0.41	0.45	0.40
Efficiency	100%*	111%	110%	85%	112%

CASE II(b)

Same as Case II(a) but measurement errors have the contaminated normal distribution.

n = 300 Bias	-0.43	-0.13	-0.15	0.12	-0.17
Std. Dev.	0.33	0.44	0.45	0.53	0.43
Efficiency	100%*	141%	134%	103%	141%
n = 600 Bias	-0.46	-0.15	-0.16	0.10	-0.18
Std. Dev.	0.25	0.33	0.34	0.40	0.33
Efficiency	100%*	201%	190%	159%	194%

* By definition.

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